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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of Murphy *et al.*

Serial No. 09/523,809

Filed: March 13, 2000

For: Bioengineered Tissue Constructs and Methods for Producing and Using Thereof

Group Art Unit: 1633

Examiner: C. Stroup

Attorney. Docket: 68603.498CON

I hereby certify that this correspondence is being deposited with the United States Postal Service as First Class Mail with sufficient postage in an envelope addressed to the Commissioner for Patents, Washington, D.C. 20231.

April 12, 2001 — Date of Signature and Mail Deposit

By Kenneth Maben — Kenneth Maben

AMENDMENT AND RESPONSE UNDER 37 C.F.R. § 1.111

Commissioner for Patents
Washington, D.C. 20231

Dear Sir:

This Response Under 37 C.F.R. § 1.111 is filed in reply to the Office Action mailed October 12, 2000, the time for responding having been extended to April 12, 2001, by the accompanying petition for a three-month extension of time. The Commissioner is authorized to debit the three-month extension of time fee of $445.00 (small entity) from Deposit Account No. 08-0219. The Commissioner is also authorized to debit any fee that may be required to maintain the pendency of this application from Deposit Account No. 08-0219.

Applicants respectfully request reconsideration and reexamination of the above-referenced patent application in view of the following amendments and remarks.

Amendments to the Specification

Please amend the specification as described below. As required by 37 C.F.R. § 1.121(b)(1) the amended paragraphs are rewritten with all changes included. In addition, also attached, is a marked-up version of the amended paragraphs, marked to show all of the changes relative to the previous version.

CF 8/13/10

Please add the following title and paragraph on page 1, between lines 2 and 3.

CF 8/13/10 On pages 20-21, please delete the paragraph at lines 12-30 and 1-~~14~~ 2 and replace it with the following paragraph:

As mentioned above, the system for the production of a cell-matrix construct may be used in the formation of a corneal construct. The corneal epithelial cells can be derived from a variety of mammalian sources. The preferred epithelial cell is a rabbit or human corneal epithelial cell (corneal keratinocyte) but any mammalian corneal keratinocyte may be used. Other epithelial keratinocytes such as those derived from the sclera (outer white opaque portion) of the eye or epidermis may be substituted, but corneal keratinocytes are preferable. In the method for forming a corneal construct, the medium is removed from the culture insert (containing the cell-matrix construct) and its surround. Normal rabbit corneal epithelial cells are expanded via subculture, trypsinized to remove them from the cultures substrate, suspended in culture medium, and seeded on top of the membrane at a density between about 7.2 x 10^4 to about 1.4 x 10^5 cells/cm^2. The constructs are then incubated without medium for about four hours at 37 ± 1°C, 10% CO_2 to allow the epithelial cells to attach. After incubation, the constructs are submerged in Corneal Maintenance Medium (CMM) (Johnson et al., 1992.) The epithelial cells are cultured until the cell-matrix construct is covered with the epithelial cells. Completeness of epithelial coverage can be ascertained by a variety of methods, for illustration by staining the culture with a solution of Nile Blue sulfate (1:10,000 in phosphate buffered saline). Once the cell-matrix construct is covered, after approximately seven days, the constructs are aseptically transferred to new culturing trays with sufficient corneal maintenance medium (CMM) to achieve a fluid level just to the surface of the construct to maintain a moist interface without submersion of the epithelial layer. The constructs are incubated at 37 ± 1°C, 10% CO_2, and greater than 60% humidity, with the CMM, making media changes, as necessary, typically, three times per week.